REMARKS

Reconsideration of this Application is respectfully requested. Claims 13, 24, 26, and 27 have been canceled without prejudice. The subject matter of Claims 1, 2, and 25 have been amended to more particularly point out and distinctly claim the subject matter of the invention. In particular, the characteristics of Claim 26 have been incorporated into Claim 25. Support for the amendments to the claims can be found throughout the Specification as originally filed, including in the original claims. No new matter has been entered. If the proposed Amendments to the claims are entered, Claims 1-10, 12, 15-23, 25 and 28 will remain for consideration. Reconsideration of this Application is respectfully solicited.

Rejections under 35 U.S.C.§ 112, first and second paragraph:

The Examiner has rejected Claims 24[1] and 27 for an asserted failure to meet the Written Description requirement. The Examiner asserts that the Specification, as originally filed, did not provide support for, "one or more antigens". The Examiner has also rejected Claim 27 asserting that it lacks proper antecedent basis.

In addition, the Examiner has rejected Claims 1-10, 12, 13, 22, 23, and 28 as being indefinite. The Examiner objects to the phrase, "consisting essentially of" because the Examiner asserts that the phrase is ambiguous and ill-defined. In particular, the Examiner asserts that it is not clear whether the phrase, "consisting essentially of" includes the addition of a cytokine.

The Examiner further asserts that Claim 1 is indefinite for stating, "an immunogenic composition" because the Examiner asserts that since the adjuvant and antigen are joined together the claim reads as a compound.

The Applicant respectfully traverses the Examiner's rejection. Claims 1, 2, and 25 have been amended to more particularly point out and distinctly claim the subject matter of the invention. In particular, Claims 24 and 27 have been canceled solely to expedite the allowance

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[1] The Applicant has assumed that the Examiner actually meant Claim 24 rather than Claim 25 as indicated in the Office Action, since Claim 27 is dependent on Claim 24, and Claim 24 contains the phrase the Examiner has objected to.

of the remaining claims. However, the Applicant continues to hold that upon careful review of the instant Specification at the time that the present Application was filed a skilled artisan could only conclude that the Applicant had possession of the subject matter of now canceled Claims 24 and 27.

On the other hand, the Applicant fully agrees with the Examiner that Section 2111.03 of the MPEP clearly defines the transitional phrase "consisting essentially of". Furthermore, the Applicant wishes to explicitly place on the record that the instant Claims are written with this definition in mind and therefore, the metes and bounds of the claims of the present invention are clearly defined.

Thus, as the MPEP states, the transitional phrase, "consisting essentially of" limits the scope of the claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention [citing *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976)]. Therefore, claims that contain the transitional phrase "consisting essentially of" are not intended to further comprise a "cytokine". Accordingly, the Applicant has canceled Claim 13 so as to comply with 35 U.S.C. §112, paragraph four.

Finally, the Applicant respectfully points out that a composition can consist essentially of two elements that are linked together. For example, the Applicant respectfully suggests that a polysaccharide cross-linked to a protein is better defined as a composition than as a compound, whereas a fusion protein comprising an adjuvant and an antigen can arguably be defined in either manner. Since the claims include both of these possibilities, the Applicant respectfully suggests that the term "composition" may be the more appropriate term.

In view of the above and foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first and second paragraph are respectfully solicited.

Rejection under 35 U.S.C. §102(e):

The Examiner has rejected Claims 1-4, 8-10, 12, 13, 15, 16, 24, and 27 as being anticipated under 35 U.S.C. §102(e) by Mond *et al.* (U.S. Patent No. 5,874,085). The Examiner has also maintained the rejection of Claims 1-4, 8-10, 12, 13, 15 and 16, as being anticipated

under 35 U.S.C. §102(e) by Mond *et al.* (U.S. Patent No. 5,932,427) and has extended this rejection to include Claims 24 and 27.

The Examiner asserts that the '085 patent contains complexes that include CD40L and a bound antigen (particularly citing Columns 10 and 11 and Columns 16, Table 2 of the '085 Patent). The Examiner further asserts that the Applicant has "mischaracterized " the '085 Patent by quoting Column 3, lines 32-34 as stating that stimulants such as lypopolysaccharide (LPS) and CD40 ligand activate B cell proliferation and Ig secretion without isotype switching. The Examiner refers to lines 35-49 of Column 3 from the '085 Patent as stating that such stimulants may permit switching to occur. The Examiner then asserts that the prior art (*i.e.*, the '085 Patent) teaches the ability of the CD40 ligand to induce class switching.

Significantly, the Examiner asserts that the use of "consisting essentially of" has been interpreted to be equivalent to the use of the term "comprising" based on the asserted ambiguity of this transitional phrase (discussed above) and then appears to rely on this interpretation for the basis of at least some of the rejections under §102(e).

The Applicant respectfully traverses the Examiner's rejections for the reasons detailed in the earlier Amendments. In particular, the Applicants point out that the claimed immunogenic compositions and vaccines do not include cytokines. Therefore, as previously indicated, neither the '085 Patent nor the '427 Patent anticipate the present invention as claimed.

The portion of the '085 Patent cited by the Examiner merely states that the stimulants (*e.g.*, the CD40 ligand) "**may** permit switching to occur" (emphasis added). This statement does not support the assertion that the CD40 ligand can induce class switching, particularly in view of the topic sentence of the paragraph which states that stimulants such as lypopolysaccharide (LPS) and CD40 ligand activate B cell proliferation and Ig secretion **without** isotype switching (emphasis added). Taken together the plain meaning of the paragraph is that whereas the CD40 ligand alone does not induce isotype switching, it may not prevent an additional agent, *e.g.*, a cytokine as taught by the '085 Patent, from inducing isotype switching.

Indeed, the '085 patent teaches that a cytokine, such as exogenous cytokines TGF-β, IL-4, and either IL-5 or IL-2, is required for isotype switching. Consistently, all of the vaccine

structures and components listed in Table 2 of the '085 patent, specifically referred to by the Examiner, contain a cytokine either added in a simple admixture or conjugated to the multivalent carrier and/or antigen. In direct contrast to the '427 patent and the '085 patent, however, the claimed immunogenic compositions and vaccines of the present invention do not include an exogenous cytokine. Therefore, neither the '427 Patent nor the '085 patent anticipate the present invention.

In view of the above and foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(e) are respectfully solicited.

Rejection under 35 U.S.C. §103:

The Examiner has also rejected Claims 1-10, 12, 13, and 15-28 as being obvious over U.S. Patent Nos. 5,874,085 (Mond *et al.*) and 5,932,427 (Mond *et al.*), in view of U.S. Patent Nos. 5,247,069 (Ledbetter *et al.*) and 5,961,974 (Armitage *et al.*), and further in view of the known methods in the art.

The Examiner has basically repeated the arguments presented in the earlier Office Actions. Thus, the Examiner asserts that Ledbetter *et al.* (Patent No. 5,247,069) teach the use of Bp50-specific antibodies as adjuvants, and that Armitage *et al.* teach that oligomeric CD40 ligands and cross-linked anti-CD40 antibodies are agonistic. The Examiner also asserts that it was known that the antibodies were useful as vaccine adjuvants. The Examiner further asserts that since B cells serve as antigen presenting cells the use of anti-CD40 antibodies would have been expected to serve the dual role of delivering to the appropriate cell type for antigen presentation and antibody production. The Examiner summarizes his argument by asserting that since Armitage *et al.* and Ledbetter *et al.* teach either CD40L or antiCD40 antibodies can serve as cytokines, and asserting that Mond *et al.* teach the conjugation of antigens to adjuvants, it would have been obvious for the skilled artisan to combine these teachings ("in the absence of additional cytokines") to make the immunogenic compositions and the fusion constructs of the present invention.

Finally, the Examiner asserts that the kits comprising the cells and nucleic acids encoding

the immunogenic compositions (including fusion proteins comprising the CD40 ligand/anti-CD40 antibody and antigen) are also obvious in view of the cited art.

The Applicants respectfully traverse the Examiner's rejections. Mond *et al.*, ('085 and '427) not only do not anticipate the present invention, they teach away from the present invention. Indeed, Mond *et al.*, teach that the CD40 ligand activates B cell proliferation and Ig secretion without isotype switching, and that an exogenous cytokine is required for isotype switching (see above).

Ledbetter *et al.* ('069), cannot cure this deficiency. Indeed, as stated previously, Ledbetter *et al.*, teaches that the anti-Bp50 mAb (which the Examiner has pointed out corresponds to the anti-CD40 antibody) **could not** activate B-cells (*see* Column 18, line 21). The Examiner asserts that Ledbetter *et al.* teaches the use of Bp50-specific antibodies as adjuvants and that the anti-Bp50 antibodies mimic the activity of other B cell growth factors (citing the overlapping sentence for Columns 19-20). However, Ledbetter *et al.* are simply making the point that Bp50 could function as the BCGF receptor and do not contradict their earlier statement that the anti-Bp50 mAb could not activate B-cells. Therefore, the '069 patent also teaches away from the present invention.

Armitage *et al.* ('974) also cannot cure the deficiency. As stated previously, Armitage *et al.* simply teach the sequences of the CD40 ligand (CD40-L), antibodies (particularly monoclonal antibodies) which recognize the CD40 ligand and pharmaceutical compositions that comprise these antibodies. The Examiner asserts that Armitage *et al.* teach that cross-linked anti-CD40 antibodies are agonistic and that CD40 agonists are useful as vaccine adjuvants (Columns 9-10). However, Armitage *et al.* states that anti-CD40 antibodies require IL-4 and cross-linking to mediate B-cell proliferation and immunoglobulin secretion (*see* Column 5, lines 57-62). Therefore, the present invention is also not obvious in view of Armitage *et al.*

Indeed, the skilled artisan is only brought to the present invention by the Applicant's own disclosure. Thus, in the absence of the teachings of the instant Specification, antigen-anti-CD40 conjugate would not have been predicted to be effective in enhancing immune responses since it would have been anticipated that the conjugate would be processed by the antigen presenting cell

into short peptides for MHC class II presentation, and thereby unable to stimulate B cells through the CD40 receptor. However, unexpectedly, the vaccines of the present invention were disclosed to promote both Ig secretion and isotype switching. Neither Mond *et al.*, '(085), Mond *et al.*, ('427), Armitage *et al.*, ('974), nor Ledbetter *et al.*, ('069) alone or when taken together teach toward this unexpected result, and therefore the present invention is not obvious in view of Mond *et al.*, '(085), Mond *et al.*, ('427), Armitage *et al.*, ('974), nor Ledbetter *et al.*, ('069) with or without the known methods in the art.

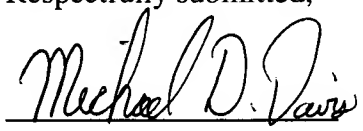
In view of the above and foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103 are respectfully solicited.

In view of the foregoing amendments and remarks, reconsideration and early allowance of Claims 1-10, 12, 15-23, 25 and 28 are respectfully requested.

No additional fees are believed to be necessitated by the foregoing amendments. However, should this be erroneous, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages. Should the Examiner feel that a telephone conference would facilitate resolution of any of the above issues, he is invited to telephone the undersigned attorney.

In view of the above and foregoing, reconsideration and withdrawal of the outstanding grounds of rejection and early allowance of the claims as amended is believed to be in order and are respectfully solicited.

Respectfully submitted,



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PENDING CLAIMS AFTER JANUARY 30 , 2001

1. (Four Times Amended) An immunogenic composition consisting essentially of an adjuvant and an antigen joined together;

wherein said adjuvant is selected from the group consisting of an antibody that binds cell surface receptor CD40, a part of said antibody that is effective at binding CD40, and a CD40 ligand; and

wherein when said adjuvant binds to CD40 of a B-lymphocyte cell said adjuvant helps in activating said B-lymphocyte cell.

2. (Three times Amended) A vaccine consisting essentially of an adjuvant and an antigen joined together;

wherein said adjuvant is selected from the group consisting of an antibody that binds cell surface receptor CD40, a part of said antibody that is effective at binding CD40, and a CD40 ligand;

wherein when said adjuvant binds to CD40 of a B-lymphocyte cell said adjuvant helps in activating said B-lymphocyte cell; and

wherein the vaccine promotes Ig secretion and isotype switching.

3. (Amended) A vaccine according to Claim 2 wherein said antigen is a T-cell dependent or T-cell independent antigen, or part of said T-cell dependent or T-cell independent antigen.

4. (Amended) A vaccine according to Claim 2 wherein said adjuvant is a CD40 ligand.

5. (Amended) A vaccine according to Claim 2 wherein said adjuvant is an antibody raised against said CD40, or a part of said antibody that is effective at binding CD40.

6. A vaccine according to Claim 5 wherein the antibody is monoclonal.

7. A vaccine according to Claim 5 wherein the antibody is humanised.

8. A vaccine according to Claim 3 wherein said antigen is soluble.

9. A vaccine according to Claim 3 wherein said antigen is a protein.

10. A vaccine wherein said antigen is a polysaccharide.

12. (Amended) A vaccine according to Claim 3 wherein said antigen is a protein or part thereof, and said antigen is fused to said adjuvant so as to provide a fusion protein.

15. (Twice Amended) A method for the manufacture of a vaccine capable of enhancing immunity comprising

(a) selecting a suitable T-cell dependent and/or T-cell independent antigen, or parts thereof, and

(b) associating or combining said antigen with an adjuvant; wherein said adjuvant is selected from the group consisting of an antibody that binds cell surface receptor CD40, a part of said antibody that is effective at binding CD40, and a CD40 ligand;

wherein when said adjuvant binds to CD40 of a B-lymphocyte cell said adjuvant helps in activating said B-lymphocyte cell; and

wherein the vaccine promotes Ig secretion and isotype switching.

16. A method according to Claim 15 wherein said vaccine is capable of enhancing T-cell independent immunity.

17. (Twice Amended) A kit for the manufacture of a vaccine capable of enhancing T-cell independent or T-cell dependent immunity comprising a cell expressing a selected T-cell dependent and/or T-cell independent antigen, or parts thereof, and an adjuvant selected from the group consisting of an antibody that binds cell surface receptor CD40, a part of said antibody that is effective at binding CD40, and a CD40 ligand;

wherein when said adjuvant binds to CD40 of a B-lymphocyte cell said adjuvant helps in activating said B-lymphocyte cell; and

wherein the vaccine promotes Ig secretion and isotype switching.

18. (Amended) A kit according to Claim 17 wherein said vaccine is capable of enhancing T-cell independent immunity.

19. (Amended) A kit according to Claim 17 wherein one or both of said antigen and adjuvant is provided with a secretion signal whereby expression of one or both of said antigen or adjuvant results in secretion of one or both of said antigen or adjuvant from said cell.

20. (Amended) A kit according to Claim 17 wherein the expression of said antigen and adjuvant is adapted such that a single fusion protein can be manufactured by said cell.

21. (Amended) A kit according to Claim 20 wherein said single fusion protein is adapted for secretion from said cell.

22. (Amended) A nucleic acid molecule encoding the fusion protein according to Claim 12.

23. A nucleic acid molecule encoding a vaccine according to Claim 2.

25. (Amended) A vaccine comprising an adjuvant and an antigen that are joined together;

wherein said adjuvant is selected from the group consisting of an antibody that binds cell surface receptor CD40, a part of said antibody that is effective at binding CD40, and a CD40 ligand;

wherein when said adjuvant binds to CD40 of a B-lymphocyte cell said adjuvant helps in activating said B-lymphocyte cell;

wherein the vaccine promotes Ig secretion and isotype switching; and

wherein the vaccine does not comprise an exogenous cytokine.

28. A vaccine according to Claim 12 wherein said adjuvant is either an antibody that binds cell surface receptor CD40, or a part of said antibody that is effective at binding CD40.